

## **REMARKS**

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

### **I. CLAIM STATUS AND AMENDMENTS**

Claims 3-7 and 10 were pending in this application when last examined and stand rejected.

Claim 4-7 were objected to.

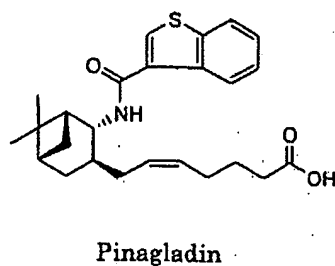
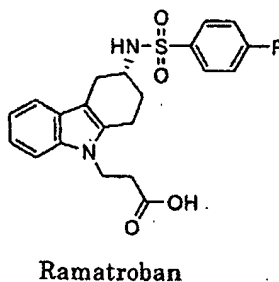
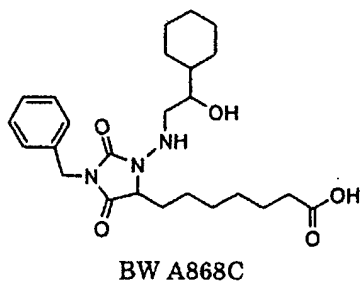
Claims 3 and 10 are amended. Support for these amendments can be found throughout the specification. In particular, Ramatroban (see Example 6 and Fig. 27) and TM 30089 are CRTH2-type receptor antagonists while BW A868C, Pinagladin and ONO-4127 are DP-type receptors.

No new matter has been added.

### **II. ENABLEMENT REJECTION**

On page 5 of the Office Action, claims 3 and 10 were rejected under 35 U.S.C. § 112, first paragraph, for not reasonably providing enablement for the genus of prostaglandin D receptor antagonist. Applicants respectfully traverse this rejection.

In Examples 6 and 7 in the specification, three prostaglandin D receptor (DP receptor) antagonists, BW A868C, Ramatroban and Pinagladin, all of which are useful for the treatment and prevention of brain injury while having different chemical structures, are described. These three prostaglandin D receptors are shown below:



In addition to the above-noted three DP receptor antagonists, two additional DP receptor antagonists were evaluated on whether they can treat brain injury.

Specifically, the effect of **TM30089** (3-[(4-fluoro-benzenesulfonyl)-methylamino]-1,2,3,4-tetrahydro-carbazol-9-yl}-acetic acid) or **ONO-4127** Na (-(pbutoxy)benzoyl-2-methylindole-4-acetic acid), which are known to be the antagonist of prostaglandin D receptors was evaluated on a model of stab-wounded brain injury by a leakage amount of dye to the injured area (Kamimura et al., Nature Medicine, 1998, 4:1078-1080). It was found that the increase in amount of leaked dye noted as a result of brain injury was also suppressed. Enclosed with the reply of December 16, 2008 was a Declaration by Dr. Yoshihiro Urade presenting experimental data to support these findings. The Office is respectfully requested to consider and enter this Declaration.

It was found that when hereditary or traumatic brain injuries occurs, expression of H-PGDS and DP receptor increase (see Example 3, page 2, lines 24-25, of the specification), and that when an antagonist for DP receptor is administered, the expression of DP receptor decreases (page 3, lines 3-5, of the specification), resulting in reduction of traumatic brain injury (Examples 6 and 7 in the specification).

Thus, it is reasonable to a person of skill in the art that the claimed genus of DP-type and CRTH2-type prostaglandin D receptor antagonist can reduce brain injury caused by prostaglandin D receptor activity without undue experimentation.

Therefore, the specification provides enablement for claimed genus of prostaglandin D receptor antagonists.

For the above-noted reasons, this rejection is untenable and should be withdrawn.

### **III. OBVIOUSNESS REJECTION**

On pages 12-14, claims 3-7 and 10 were rejected under 35 U.S.C. § 103(a) as obvious over Tsuru et al. in view of Wong. Applicants respectfully traverse this rejection for the reasons given in the December 16, 2008 response.

Applicants again note that based on references 1-5 given in the December 16, 2008 reply, a person of skill in the art would have no reasonable expectation of success in using the claimed compounds to inhibit brain injury based on the finding that a compound was effective for treating edema of nose and respiratory organs.

Thus, for the above-noted reasons and for the reasons of record, this rejection, as applied to the amended claims is untenable and should be withdrawn.

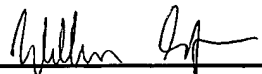
**CONCLUSION**

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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